Date:	4 October 2004	
To:	David Goldman, M.D.	Chair, IRB, NIAAA
Recommended by:	_____	Clinical Director, NIAAA
	_____	Chief, LCTS, NIAAA
Protocol title:	Assessment and treatment of people with alcohol drinking problems	
Abbreviated title:	Alcoholism treatment and assessment	
Identifying words:	CIWA, Addiction severity index, CPRS-S-A, cognitive behavioral therapy, motivational enhancement therapy	
Principal Investigator:	Markus Heilig, M.D., Ph.D.	

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Estimated duration of study:	Five years

Subjects of study

Number	Gender	Age range
1000	Male	18-65 yr
1000	Female	18-65 yr

Project uses ionizing radiation:	No
Project involves use of Durable Power of Attorney	No
Off-site project:	No
Multi-institutional project:	No

1. Précis

The purpose of this protocol is to create a mechanism whereby the intramural program of the NIAAA can evaluate and treat a broad range of people with drinking problems at the NIH Clinical Research Center (CRC) in Bethesda, MD. Through this program, subjects will receive standard treatment for their clinical alcohol, psychosocial and medical problems and the program will be able to evaluate and recruit subjects for other, more focused clinical research efforts to advance its research goals. Additionally, this will allow investigators and staff to gain broad training experience in alcohol and addiction medicine through the clinical care of such patients. The protocol is open to any adult who is seeking help for a drinking problem and who is qualified to participate, basically presenting to the CRC in a reasonably stable medical and psychiatric condition. Subjects will be recruited through local media and professional avenues in the Washington, DC Metro area. They will be evaluated by a nurse and physician, among others, who will determine the need for hospitalization, detoxification and to address other issues. For those needing medically supervised detoxification, a standard program of monitoring and treatment with benzodiazepines and other medications will be instituted. A standard battery of screening blood and urine tests, an electrocardiogram and chest x-ray will be done as part of the comprehensive medical assessment. Following at least five days of abstinence from alcohol, subjects will undergo a series of verbal and observational-type assessments designed to evaluate psychiatric co-morbidity, psychopathology, psychosocial problems, personality and other factors relevant to alcoholism treatment. Subjects will then be offered a 12-week course of treatment as an outpatient. The treatment program consists of either cognitive behavioral-based counseling (cognitive behavioral therapy- or CBT) which is designed to improve coping skills in problem areas, motivational enhancement therapy (MET), designed to produce and strengthen internal motivations to remain alcohol-free, manual based “medical management” (MM) ???. During the outpatient phase, at weeks 1, 2, 6 and 12, subjects will have selected blood and body fluid tests and interviews done to evaluate abstinence from alcohol and verbal/observational assessments to identify change in various psychological dimensions. During their participation in this protocol, subjects will be approached to consider enrolling in other clinical research protocols such as imaging studies and drug-treatment trials. Cosent for this will be obtained separately if agreeable.

2. Introduction

People who have serious problems related to alcohol drinking have heterogeneous historical courses, some of which may come to clinical attention [1]. Some people experience resolution of their drinking problems with or without professional or personal help, while others go through variable cycles of adverse consequences, treatments and other efforts at abstinence or reduced drinking, lapse (first drinking episode) and relapse (recurring sustained heavy drinking episode) and re-mergence ? of old and new untoward consequences [1]. It is in recognition of this cycle that alcoholism, here equated with alcohol dependence, has been dubbed a chronic, relapsing disease, analogous in some respects to diabetes[1-3]. However, as medical, psychiatric and psychological research has advanced, the understanding of how alcohol affects the body’s (brain and other systems) health and how coping difficulties maintain problem drinking and, indeed, the concept of disease itself are changing [4].

Against this changing knowledge, treatments for clinically manifest alcohol problems are emerging. The most commonly employed psychosocial treatment options, cognitive-behavioral coping skills therapy, motivational enhancement therapy, and twelve-step facilitation, are equally effective with abstinence rates of 19-35% and relapse rates of 40-46% at one year, under optimal conditions, delivered either in inpatient, day treatment, residential or outpatient settings [5, 6]. Neuro-pharmacological treatments are being increasingly studied; thus far two drugs, naltrexone and acamprosate, have demonstrated benefit [7-9]. Both are to be used in conjunction with counseling and supportive approaches, where they yield abstinence rates at one year of (17-47%), with most relapse occurring at three months (35-60% relapsed) under typical clinical trial conditions [10-12]. Furthermore, response to treatment in "real-world" care delivery environments is very sparsely documented [13].

Given the challenges of understanding and treating the clinical problems of alcoholism, alcohol abuse and dependency, the primary thrust of the Laboratory of Clinical and Translational Studies (LCTS) at the intramural research program of the NIAAA is to investigate the neurochemistry of alcohol dependency and withdrawal (which itself may play a role in relapse), mechanisms of relapse and craving and their possible inter-relationship and the short-term efficacy of candidate drugs in promoting abstinence. The main approaches used by the LCTS are translational research from pre-clinical to clinical models using sensitive observational techniques and tools, collaborations with other intramural scientists and scientifically sound and relevant clinical research projects.

For this final approach, the NIAAA intramural program needs a steady base of subjects who are seeking treatment for problems related to alcohol drinking and willing to participate in clinical studies. Furthermore, a busy and broadly-based alcoholism unit supports another important program goal: to train clinicians and investigators in alcohol studies.

One of the most important activities of such a clinical service, after withdrawal of alcohol, is a comprehensive, iterative assessment of an individual's status, including psychiatric and medical conditions, psychosocial functioning and frame of mind [1]. Assessments also provide baseline data that can be used to control and stratify analyses in subjects who participate in subsequent clinical research. For example, psychiatric co-morbidity, patient motivation, gender and severity of sociopathy all have significant effects on drinking behavior targeted in a clinical trial [3, 14].

To provide the framework for operational management of the LCTS research program and conducting clinical trials in coordination with the NIH CRC operation and to achieve the goal of recruiting subjects for research, we have written this protocol as a hybrid screening and short-term natural history protocol. Through it we offer patients supervised detoxification from alcohol, comprehensive assessment of their problems and a three-month course of a standard psychosocial treatment for alcoholism using methodology with documented efficacy. Within this framework, we will seek subject participation in other protocols focused on more specific questions, including those related to alcohol withdrawal and the neuropharmacology of relapse (prevention).

3. Objectives

Objectives of the protocol

This protocol has several purposes:

1) It is meant to serve as an entry mechanism to authorize a subject's admission to the NIH CRC in Bethesda, Maryland under the care of the NIAAA LCTS and the CRC 1SE nursing staff inpatient and outpatient care unit, 1SE.
2) It authorizes the provision of state-of-the-art care for individuals with alcohol and drug problems, including detoxification, assessments, and outpatient counseling approaches.
3) It provides a set of standard measures, serving a dual purpose:
    a. To provide a basis for optimal treatment planning / maching, and followup, for the benefit of the individual patient
    b. To potentially provide, for patients who consent to participation in other NIAAA research protocols and the use of these data, patient characteristics and follow up measures relevant for these protocols
4) It can serve as a reference document for community facilities that may be interested in referring clients to the NIAAA intramural program.

4. Study Design and Methods

This protocol does not involve experimental procedures or therapeutics. Rather, it follows the typical clinical course of events in people with alcohol dependency and abuse over a brief, intensive time period. It therefore consists of a series of phases including: phone intake, baseline, and outpatient treatment (Figure 1). In summary, the planned procedures throughout this protocol involve routine verbal and observational procedures, such as "pen-and-paper"-style self-reports and interviews, and minimally invasive procedures, such as phlebotomy and urine collection, electrocardiogram (ECG) and chest x-ray (CXR) to provide a comprehensive medical, psychiatric and addiction medicine evaluation. The treatment involves standard outpatient counseling-type therapy for alcohol dependency.

Following recruitment to the CRC, subjects will be examined by the medical and nursing staff to determine medical and psychiatric stability and to evaluate inclusion and exclusion criteria. Selected blood and body fluid tests, among others, may need to be done, upon first encounter depending on clinical findings.

Subjects may need to be hospitalized for monitoring and treatment for problems and certain conditions, such as alcohol withdrawal, which, when uncomplicated, typically lasts about a week [15, 16]. The standard treatment for alcohol withdrawal is supportive, with occasional need for medications, usually benzodiazepines, guided by the Clinical Institute Withdrawal Assessment-Alcohol Revised (CIWA-AR), a validated tool that categorizes the severity alcohol withdrawal based on symptoms and physical signs [16]. Severe alcohol withdrawal and dehydration will be treated in standard medical fashion. Furthermore, intravenous fluids and parenteral medications may be required. This phase begins the baseline period.

After subjects are detoxified, during the baseline period, they will undergo various verbal and observational assessments (detailed below). Based on these assessments, treatment planning will be undertaken by the multidisciplinary team, and with the active participation of the patient. They will then be offered an opportunity to enroll in a three-month treatment course of counseling that would consist of one of the following: cognitive-behavioral coping skills (CBT) or motivational enhancement therapy (MET) MM? run through the NIAAA/CRC outpatient clinic (see below). Alternatively, they

may be referred to a suitable non-NIH program for further treatment, depending on their preferences and treatment availabilities.

During the outpatient follow-up phase they will also be seen for brief medical and psychiatric check-ups on outpatient phase weeks 1, 2, 6 and end-of-therapy, at which time some blood and body fluid tests will be performed, as well as selected verbal assessments (see below).

The assessment instruments; blood, body fluid and body tests; and therapies, with schedules are:

A. Structured assessments of a subject's history and internal psychologic experiences are performed using pen-and-paper and computerized tools.
    a. The Addiction Severity Index (ASI) is an instrument used extensively in the Addiction Medicine field to comprehensively identify problems in multiple dimensions including medical, employment, drug and alcohol use, legal, family and social and psychiatric [17]. It is a 200-item interview that takes about 60 minutes. It will be done prior to and at the end of the outpatient treatment phase, i.e. baseline and end-of-therapy.
    b. The Structured Clinical Interview for Diagnostics and Statistics Manual-IV (DSM-IV) (SCID-I) is another widely-used, standard clinical interview to establish criteria for psychiatric diagnoses [18]. It is a structured interview consisting of 11 modules with between 35-292 items/module that takes about 120-180 minutes. It will be done at baseline.
    c. The Obsessive-Compulsive Drinking Scale (OCDS) assesses craving and urges for alcohol [19]. It is a 10-item self-report that takes about 5-10 minutes. It will be done at baseline and at weeks 1, 2, 6 and end-of-therapy during the outpatient treatment phase.
    d. The affective symptoms (anhedonia, depression, anxiety, and dysphoria) following removal of alcohol and other drugs, the so-called motivational effects of alcohol, will be assessed with self-administered subscales derived from the Comprehensive Psychopathological Rating Scale Self-rating Scale for Affective Syndromes (CPRS-S-A) [20, 21]. It is a 19-item self-report that takes 5-10 minutes to complete. It will be done twice weekly during the baseline and, if applicable, outpatient phase.
    e. The Timeline Follow-Back (TLFB) technique collects drinking information using personal historical events recounted over a fixed preceding time period [22, 23]. It is a commonly used technique to assess alcohol drinking patterns and quantification in treatment programs. The number of items corresponds to the number of days of interest, up to 360 which usually takes about 30 minutes. It will be done at baseline to cover the prior 360 days and at weeks 1, 2, 6 and end-of-therapy.
    f. The Neurotocism-Extroversion/Introversion-Openess to Experience (Five Factor) Personality Inventory- Revised (NEO PI-R) provides scores on various dimensions of personality [24-26]. It is a 240-item self-report that takes up to 35-45 minutes to complete. It will be done at baseline.
    g. The Wechsler Adult Intelligence Scale-Revised (WAIS-R) is the standard technique to determine Intelligence Quotient (IQ). We use the Block Design and Vocabulary components to measure IQ. In total the tasks

comprise 50 items that take about 15-30 minutes to complete. It will be done at baseline.

h. Several cognitive factors associated with alcohol use and treatment readiness are measured with a variety of instruments. These include:
    i. The [University of Rhode Island Change Assessment Scale (URICA) [27] or the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) [28]] is used to indicate a subject's motivation and readiness for treatment. [The URICA is a 32-item self-report that takes about 5-10 minutes. The SOCRATES is a 19-item self-report that takes about 3 minutes.] It will be done at baseline.
    ii. The Alcohol Expectancies Questionnaire (AEQ) is a measure of beliefs about the effects or outcomes of drinking [29]. The AEQ is a 120-item self-report that takes about 10-15 minutes. It will be done at baseline and week 12 of outpatient therapy. It will be done at baseline and end-of-therapy.
    iii. The Alcohol Abstinence Self-Efficacy Scale (AASE) is a measure of self-efficacy, or the level of confidence concerning the ability to resist engaging in drinking behavior, offering an assessment of coping skills [30]. It is a 40-item self-report that takes about 10 minutes. It will be done at baseline and weeks 1, 2, 6 and end-of-therapy
    iv. The Drinking-related Internal-External Locus of Control Scale (DRIE) measures the extent that a subject believes that important outcomes in life are under personal or non-personal control[31, 32]. It is a 19-item self-report that takes about 5-10 minutes. It will be done at baseline. ? if someone in the lab has a need / interest, not otherwise

i. The Family Tree Questionnaire (FTQ) is an interview about a subject's family history of alcohol and drug problems[33]. It is an interview, with the number of items depending on the size of the population of first and second degree relatives. It takes about 5-10 minutes. It will be done at baseline.

j. The Important People and Activities Instrument (IPA) is a structured interview about interpersonal and social networks, especially as they relate to alcohol drinking [34, 35]. It covers 19 items and takes about 20-30 minutes. It will be done at baseline.

B. Bio-medical evaluations are procedures that physically analyze components of a subject's body. They include:
    a. Breath alcohol analysis, which will be done at baseline and at weeks 1, 2, 6 and end-of-therapy.
    b. Blood test panels to assess physiological functions and organ damage, as well as assessment of the extent of alcohol and drug exposure, including toxicology and biomarkers. The blood tests include:
        i. Complete blood count with differential (CBC with diff) (3 mL). It will be done at baseline and weeks 1, 2, 6 and end-of-therapy.

ii. Chem 20 Panel (Chem 20): Sodium (Na), Potassium (K), Chloride (Cl), Total CO2 (bicarbonate), Creatinine, Glucose, Urea nitrogen (BUN), Albumin, Calcium total, Magnesium total (Mg), Inorganic Phosphorus, Alkaline Phosphatase, ALT/GPT, AST/GOT, Total Bilirubin, Direct Bilirubin, LD, Total Protein, Total CK, Uric Acid, amylase. (4 mL). It will be done at baseline.
iii. Thyroid Screen: Thyroid stimulating hormone (TSH), Free thyroxine (FT4), Tri-iodothyroine (T_3) (3.5 mL). It will be done at baseline.
iv. Lipid Panel: Total Cholesterol, Triglycerides, High-Density lipoprotein (HDL) Cholesterol, Low-Density Lipoprotein (LDL) Cholesterol (3.5 mL). It will be done at baseline.
v. Viral Markers Protocol Screen: (Hepatitis B surface antigen (HBsAg), Hepatitis C Virus antibody (anti-HCV), Human Immunodeficiency Virus 1 and 2 (anti-HIV) (8 mL). It will be done at baseline.
vi. Vitamins and trace minerals (VTM): folate (serum and RBC), iron (serum iron, transferrin saturation, ferritin) ;vitamin B_{12}, vitamin C, vitamins A & E, zinc (24.5 mL). It will be done at baseline.
vii. Biomarkers: Currently, there is no clear standard set of blood and body fluid tests that clearly indicates relapse to alcohol use. However, guidelines are emerging [36].
    1. Hepatic Panel (blood, 3.5 mL). It will be done at weeks 1, 2, 6 and end-of-therapy
    2. Gammaglutamyl-transpeptidase (GGT) (blood, 3.5 mL) [37]. It will be done at baseline and weeks 1, 2, 6 and end-of-therapy.
    3. Carbohydrate-deficient transferrin (CDT) (blood, 2.5 mL) [38]. It will be done at baseline and weeks 1, 2, 6 and end-of-therapy.
    4. 5-hydroxytryptophol (5HTOL) (urine) [39]. It will be done at baseline and weeks 1, 2, 6 and end-of-therapy.
    5. Ethyl glucuronide (urine) [40]. It will be done at baseline and at weeks 1, 2, 6 and end-of-therapy. VERY GLAD TO SEE THIS ONE, AT ISBRA IT LOOKED QUITE GOOD. IS THE ANALYSIS OFFERED HERE? IF NOT WE HAVE TIES WITH A LAB THAT RUNS IT
viii. Volume of blood. A total of 102.5 mL (excluding clinically urgent blood tests) will be done over the course of the baseline evaluation (52.5 mL) and 12 weeks of outpatient therapy (50 mL). Some of the findings from these tests (for example, anti-HCV antibody (+) results) may require other tests for further clinical assessment.

c. Urine tests
    i. Urinalysis will be done at baseline and during follow-up as clinically indicated.
    ii. Urine drug screens

1. The Qualitative (DLM) tests for benzodiazepines, cocaine, methamphetamines, opiates and tetrahydrocannabinol (THC). It provides a result within hours. It will be done at baseline and weeks 1, 2, 6 and 12.
2. The Drug Profile #1 tests for amphetamines, barbiturates, benzodiazepines, cocaine, lysergic acid diethylamine, opiates, phencyclidine and THC. It has greater sensitivity than the DLM screen and takes about five days to complete. It will be done at baseline and weeks 1, 2, 6, and at end-of-therapy.

iii. Pregnancy test. It will be done at baseline and at weeks 1, 2, 6 and at end-of-therapy.

iv. Biomarkers (see above)
1. 5-HTOL (see above)
2. Ethyl glucuronide (see above)

d. Other procedures used to screen for medical diseases and abnormalities.
i. An electrocardiogram (ECG) is a skin-based measurement of electrical activity occuring within the chest. It will be performed at baseline.
ii. The chest x-ray applies a very low-dose of ionizing radiation to generate an image of anatomical structures inside the chest cavity. It will be performed at baseline.

C. Therapy
a. The assessments listed above are considered to be an important component of treatment planning, indicating areas of treatment focus and monitoring [1, 41].
b. Cognitive-behavioral coping skills therapy (CBT) is a treatment approach that basically focuses on the training of interpersonal and self-management skills [4, 42]. The cumulative weight of evidence has shown it to have a specific, beneficial effect [43]. It is now considered one of the standard treatments for alcohol abuse and dependency. As conducted at the NIAAA/CRC treatment program, it will be organized on a group-style approach consisting of ten structured session conducted by two therapists. In this protocol the intended schedule for the 10 sessions is weeks 1, 2, 3, 4, 5, 6, 7, 8, 10 and 12 of the outpatient phase, although a flexible schedule is permitted.
c. Motivational Enhancement Therapy (MET) is a systematic intervention approach based on the principles of motivational psychology and designed to produce rapid internally motivated change[44]. It also has a preponderance of evidence to indicate a specific, beneficial effect and it is similarly considered a standard treatment option [43]. As conducted at the NIAAA/CRC treatment program, it will be organized on an individualized counseling approach consisting of 4 structured sessions conducted by a trained therapist. The 4 sessions are planned for weeks 1, 2, 6, and 12 of the outpatient phase, although a flexible schedule is also permitted.

d. During the outpatient treatment phase problems may arise that require counseling with trained staff such as nurse/counselors or psychiatrists.
e. Drug therapy for relapse prevention would be offered through separate clinical trial protocols.

5. Inclusion and exclusion criteria

a. Inclusion

1) Age 18 years or older
2) Are seeking help for alcohol drinking-related problems

b. Exclusion

1) Unstable or emergent medical or psychiatric conditions
2) Serious neuro-psychiatric conditions which impair judgment or cognitive function to an extent that precludes them from providing informed consent, such as acute psychosis or severe dementia (incompetent individuals).

6. Monitoring subjects and criteria for withdrawal of subjects from the study

Significant events in the natural history of alcohol abuse and dependency can have very serious consequences; they include severe depression, harm to self or others, cognitive impairment, medical illness and serious legal problems. Such events do have relevance for monitoring and withdrawal of subjects from this protocol, despite the fact that it is they would very unlikely be related to therapy or procedures performed in the protocol.

During the hospitalization treatment phase, patients are kept on a secured unit under close nurse monitoring. Alcohol withdrawal severity is monitored with hourly ? WOW THAT'S INTENSE vital signs monitoring and CIWA-Ar scoring.

During the outpatient treatment phase, subjects will be examined in clinic (as scheduled above) by nurses and physicians with training and experience in the addictions who will specifically review symptoms of depression, intent to harm self or others and a history of complications such as serious legal or domestic problems. The healthcare professionals will also review the mood ratings scales from CPRS-S-A. Subjects will be examined in greater detail for cognitive impairment and medical illness if either is suggested based on history and/or routine exam.

Withdrawal criteria

- Subjects who exhibit a deteriorating clinical condition of mood, cognitive function or physical health, or who develop a serious new medical or psychiatric condition, including prolonged hospitalization.
- Subjects who become incarcerated or who perpetrate harm to self or others.
- Non-compliance with therapy: Guidelines and strategies for handling absences from therapy sessions, lateness, lapse (first instance of drinking) and relapse (first episode of sustained heavy drinking) to alcohol and/or drug use have been established and will be used in the context of CBT and MET [42, 44]. For subjects who miss appointments, efforts will be made to establish phone or other contact to enquire about the reasons for the absence(s) and to encourage them to return to treatment. Indeed, therapists are trained to use non-compliance itself as an area of focus for treatment, to the extent that the subject stays engaged. Absolute non-compliance, for example exhibited by extensive alcohol or drug use, and repeated

absence from therapy will constitute grounds for withdrawal from the protocol. This will be at the discretion of the therapists in consultation with the Principal Investigator.
- Subjects may withdraw from the protocol at any time for any reason. If they do, NIAAA and/or CRC staff will make efforts to ensure their safety and well being.

The following subjects will be considered stopped:
- Subjects who are withdrawn
- Subjects who decide to seek treatment referral elsewhere after the detoxification and assessment period
- Subjects who successfully complete the 12-week course of therapy

7. Analysis of the study

Because this is not an hypothesis-driven protocol, descriptive statistics will be continuously monitored to assess global performance of the treatment program, including: number of subjects completing the protocol, alcohol and drug use relapse rate, major complications: trauma, violence, suicide, medical complications, psychosocial functional changes (changes in IPA and ASI parameters) and to obtain administrative information such as the demographic composition of the cohort, resource utilization (inpatient and outpatient visits, duration of stay, etc.), etc. Comparisons of such data may be made on an historical, for example annual, basis.

8. Human subjects protection

A. Rationale for subject selection

Alcohol problems occur in both men and women across all cultures. Thus, participation in our program of detoxification, assessment and treatment of alcohol problems will be open to all qualified subjects who can be accommodated. Subjects are recruited primarily from the Washington, D.C. metropolitan area through standing newspaper advertisements. A copy of the currently running ad is attached to this. Any changes to it will be subject to IRB approval. Subjects will also be recruited through outreach to healthcare organizations, particularly those that see patients with alcohol and drug problems throughout Northern Virginia, Maryland, West Virginia and the Washington, D.C. and Baltimore metropolitan areas and elsewhere in the US. Increased efforts will be made to recruit subjects from the Hispanic community. This will take the form of contacts with treatment program that serve Hispanic populations, as well as through advertising in Spanish language newspapers. Language interpreters are available for non-English speaking subjects. The intramural research program is primarily focused on alcohol-related problems in adults, thus only subjects 18 years of age and over will be enrolled.

This research is covered by a Confidentiality Certificate, issued by the Public Health Service under the authority of 42 U.S.C. 241 (d). Under this certificate, NIAAA is authorized to protect the privacy of the subjects engaged in research by withholding the subject's name and other identifying information from all persons not connected to this research, except under the circumstances specified in the consent form under the section: Information on Confidentiality.

B. Evaluation of Benefits and Risks/Discomforts

1. Benefits

To individual subjects:

1) A thorough medical and psychiatric screening examination, including dental and gynecological examinations, as indicated, may prevent long-term illness and deterioration of quality of life and identify treatable conditions.
2) Supervised medical withdrawal from alcohol can prevent the risk of seizures, delirium tremens and other neurological and medical complications. It may also help prevent the development of long-term CNS damage.
3) CBT and MET have been shown to have a specific effect on improving outcome in alcohol dependency[6, 45, 46].

Benefit to NIAAA/CRC program's mission:

1) Improved treatment program performance through feedback and formal analysis of outcomes of therapy and program subject factors (dimensions of assessments)
2) Basis for clinical training of health professionals in the field of addiction medicine, including a fellowship program for physicians
3) Consistent recruiting basis for alcohol clinical research program

Benefit to community and society

1) Source of referral and treatment for subjects with alcohol problems that impact negatively on community and society.
2) Promote the research mission of a national health initiative (NIAAA).

2. Risks/Discomforts

This research protocol authorizes only routine medical care and proposes no experimental therapies and, indeed, carries no more risk than a conventional alcoholism treatment program. It falls under the minimal risk category.

Psychologic discomfort may derive from a variety of sources, for example during the assessment period or in therapy as subjects are challenged to discuss personally sensitive issues. To the extent that they are appreciated, the feelings themselves may become the subject of therapeutic focus and a target of further monitoring, if they a persistent and compelling. Also, some of the results of blood tests may at first create anxiety, such as a positive HIV test. However, as all the conditions tested for in this protocol are manageable, it is expected that the subjects, despite their anxiety, will have medical benefit from such diagnosis.

Physical discomfort mainly would derive from the alcohol withdrawal experience, if it occurs, which is treated as described above. Phlebotomy entails no serious risk and is a relatively minor discomfort, except in individuals (roughly 5% of the population) who faint in response to a phlebotomy or anticipation thereof.

Confidentiality and information technology standards are in place at the intramural programs of the NIH campus, including the NIAAA/LCS to protect electronic repositories of patient data. It is reasonably expected that these safeguards will protect subjects' medical and personal health information, ensuring their privacy.

C. Consent process

The informed consent process will take place at the NIH Clinical (Research) Center in Bethesda, Maryland. It will follow the policies and procedures as described in Manual

Transmittal Sheet M77-2 (rev.), 7 March 2003, “Informed Consent”, from the Medical Administrative Series of The Clinical Center.

In most cases patients will present to the Outpatient Department where they will be seen by CRC nursing staff and LCS medical personnel. On rare occasions, subjects may be admitted directly to the inpatient unit. Either the Principal Investigator or an Associate Investigator will conduct the consent process. The investigator will first explain that this protocol is primarily designed to allow subjects to be treated at the NIH for alcohol problems, including gathering important information, giving appropriate standard care for medical problems, including alcohol withdrawal if necessary, and offer outpatient treatment for alcohol dependency. Also, they will be told of the nature of the research mission at NIAAA and that during their participation in this protocol that they may be asked about their willingness to participate in other research studies. The investigator will explain the current protocol in terms of the tests (pen-and-paper type and biomedical procedures) that are required, and how much time they may take, and the possible treatments that will be offered for detoxification (as needed) and alcohol dependency. They will be told of the fact that information about their alcohol and drug use and other aspects of their personal history will be sought and that some of the biomedical tests that are performed may have serious implications about their future prognosis (life expectancy and well-being) and insurability, such as HIV infection. They will further be told that this information will be stored in the CRC hospital information system as well as a secure centralized computer system maintained by the NIAAA staff. They will also be informed of the NIH confidentiality policy. Finally, they will be told of their option to voluntarily withdrawal from further participation in the protocol at any time. Signing the consent form will constitute enrollment. In keeping with standard good practice, the The protocol will be re-explained to subjects periodically after admission to the program to reassess their understanding of the nature of the protocol and treatment plan.

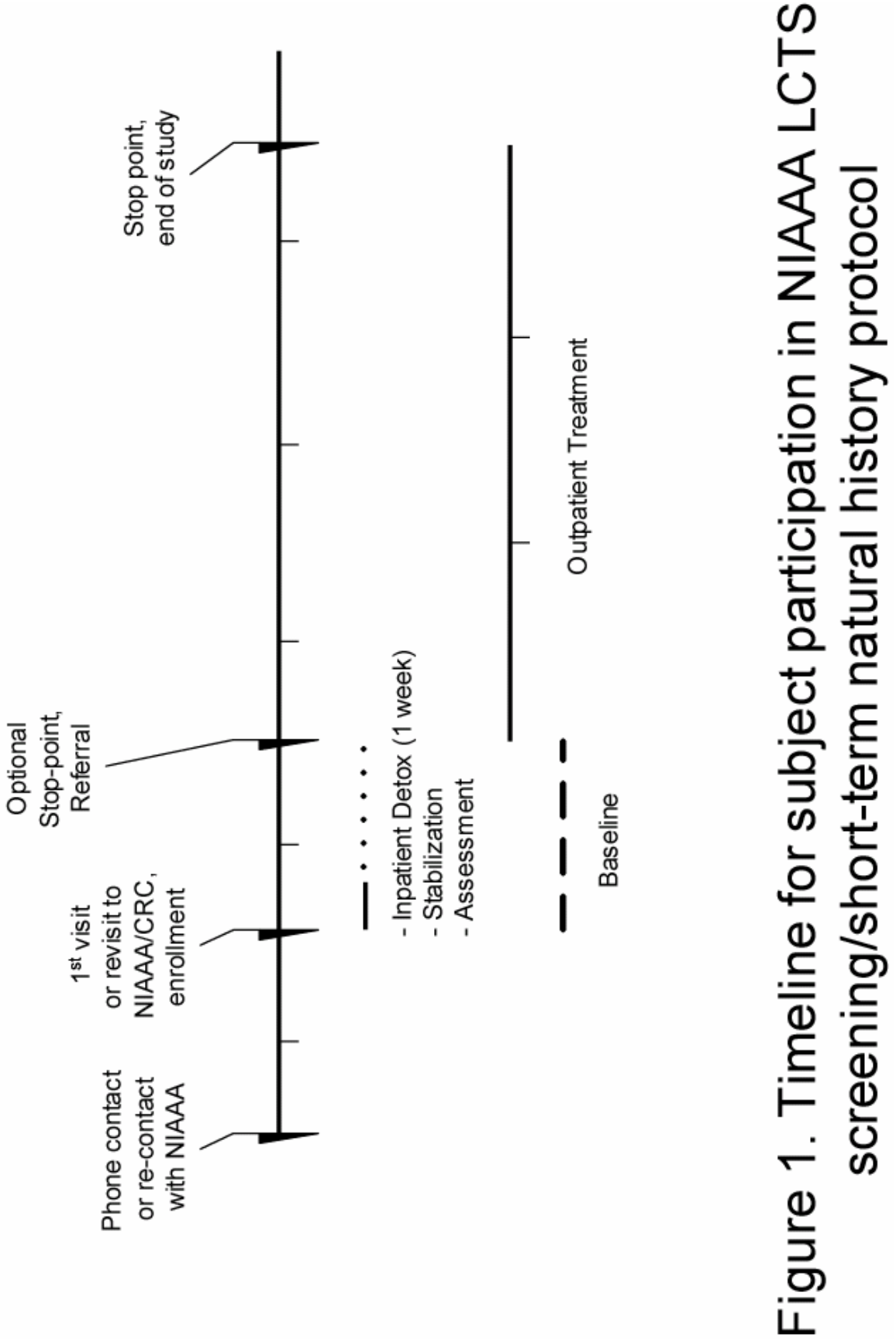

Figure 1. Timeline for subject participation in NIAAA LCTS screening/short-term natural history protocol

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